Part 2
Lecture 2 Study Design

Who I am…

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Comparing Means Between Four Groups

Review of Comparison of Two Means

Layout of Treatments

1. One Way
2. 2 by 2 Factorial

Allocation of Treatments

1. Completely Randomized Design
2. Randomized Block Design
3. Split Plot Design

A STUDY WAS DESIGNED TO INVESTIGATE THE EFFECT OF TARGET COLOUR AND PRECEEDING EXERCISE ON REACTION TIME

The study involved 24 students who played a reaction time game. A target appears on their computer screen and they click a computer key as quickly as possible.

Each game consisted of 10 targets. The program would report the mean of these ten targets.

This game was played ten times and the mean of these ten games (MEAN10) was the outcome variable used in this study.

This game was played four times. The ten targets were all red or all green. Before each game the student either carried out ten minutes of exercise or did not do. Therefore we have 2 by 2 factorial layout of treatments.

COLOUR	GREEN	GREEN	RED	RED
EXERCISE	NO	YES	NO	YES

SUBJECTS ALLOCATED IN A COMPLETELY RANDOMIZED DESIGN AND A ONE WAY LAYOUT OF TREATMENTS **(PRETEND)**

```
PROC GLM DATA = REACTION ;
CLASS GROUP ;
MODEL MEAN10 = GROUP / SS3 ;
LSMEANS GROUP/ ADJUST=T TDIFF PDIFF CL ;
RUN ;
```

The GLM Procedure

Dependent Variable: MEAN10

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	3	0.02236293	0.00745431	1.92	0.1313
Error	92	0.35654465	0.00387549		
Corrected Total	95	0.37890758			

R-Square	Coeff Var	Root MSE	MEAN10 Mean
0.059019	20.08480	0.062253	0.309953

Source	DF	Type III SS	Mean Square	F Value	Pr > F
GROUP	3	0.02236293	0.00745431	1.92	0.1313

The GLM Procedure
Least Squares Means

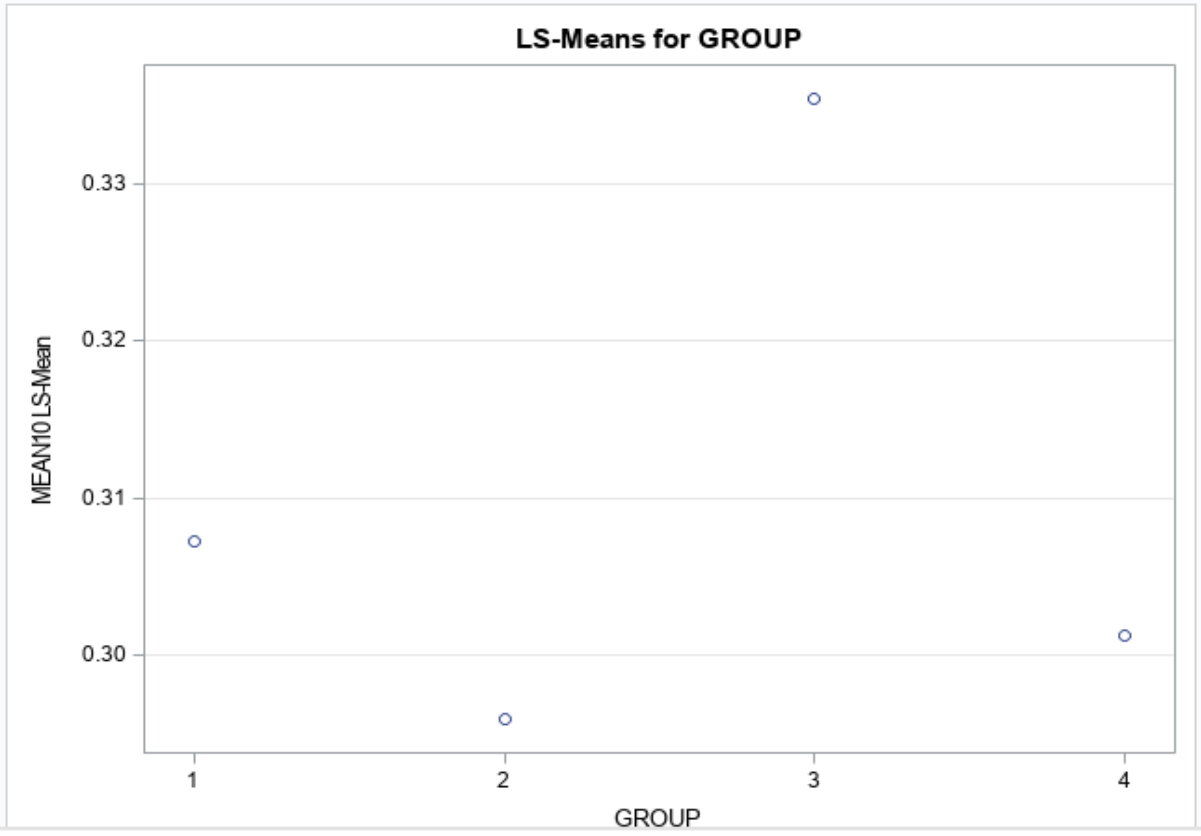
GROUP	MEAN10 LSMEAN	LSMEAN Number
1	0.30726750	1
2	0.29589083	2
3	0.33545250	3
4	0.30120042	4

Least Squares Means for Effect GROUP
t for H0: LSMean(i)=LSMean(j) / Pr > |t|
Dependent Variable: MEAN10

i/j	1	2	3	4
1		0.633057 0.5283	-1.56836 0.1202	0.337604 0.7364
2	-0.63306 0.5283		-2.20142 0.0302	-0.29545 0.7683
3	1.568359 0.1202	2.201416 0.0302		1.905963 0.0598
4	-0.3376 0.7364	0.295453 0.7683	-1.90596 0.0598	

My Note: Diff = 0.335 - 0.301 = 0.0342

Least Squares Means for Effect GROUP				
i	j	Difference Between Means	95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.011377	-0.024315	0.047069
1	3	-0.028185	-0.063877	0.007507
1	4	0.006067	-0.029625	0.041759
2	3	-0.039562	-0.075254	-0.003870
2	4	-0.005310	-0.041002	0.030382
3	4	0.034252	-0.001440	0.069944



My Note: p = 0.0598

To ensure overall protection level, only probabilities associated with pre-planned comparisons should be used !

SUBJECTS ALLOCATED IN A **COMPLETELY RANDOMIZED DESIGN** AND A 2 BY 2 FACTORIAL LAYOUT OF TREATMENTS

```
PROC GLM DATA=REACTION ;
CLASS COLOUR EXERCISE ;
MODEL MEAN10 = COLOUR EXERCISE COLOUR*EXERCISE
/SS3;
LSMEANS COLOUR          /ADJUST=T TDIFF PDIFF CL;
LSMEANS EXERCISE        /ADJUST=T TDIFF PDIFF CL;
LSMEANS COLOUR*EXERCISE/ADJUST=T TDIFF PDIFF CL;
RUN ;
```

SUBJECTS ALLOCATED IN A **COMPLETELY RANDOMIZED DESIGN** AND A 2 BY 2 FACTORIAL LAYOUT OF TREATMENTS

The GLM Procedure

Dependent Variable: MEAN10

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	3	0.02236293	0.00745431	1.92	0.1313
Error	92	0.35654465	0.00387549		
Corrected Total	95	0.37890758			

R-Square	Coeff Var	Root MSE	MEAN10 Mean
0.059019	20.08480	0.062253	0.309953

Source	DF	Type III SS	Mean Square	F Value	Pr > F
COLOUR	1	0.01249190	0.01249190	3.22	0.0759
EXERCISE	1	0.00673132	0.00673132	1.74	0.1908
COLOUR*EXERCISE	1	0.00313971	0.00313971	0.81	0.3704

The GLM Procedure
Least Squares Means

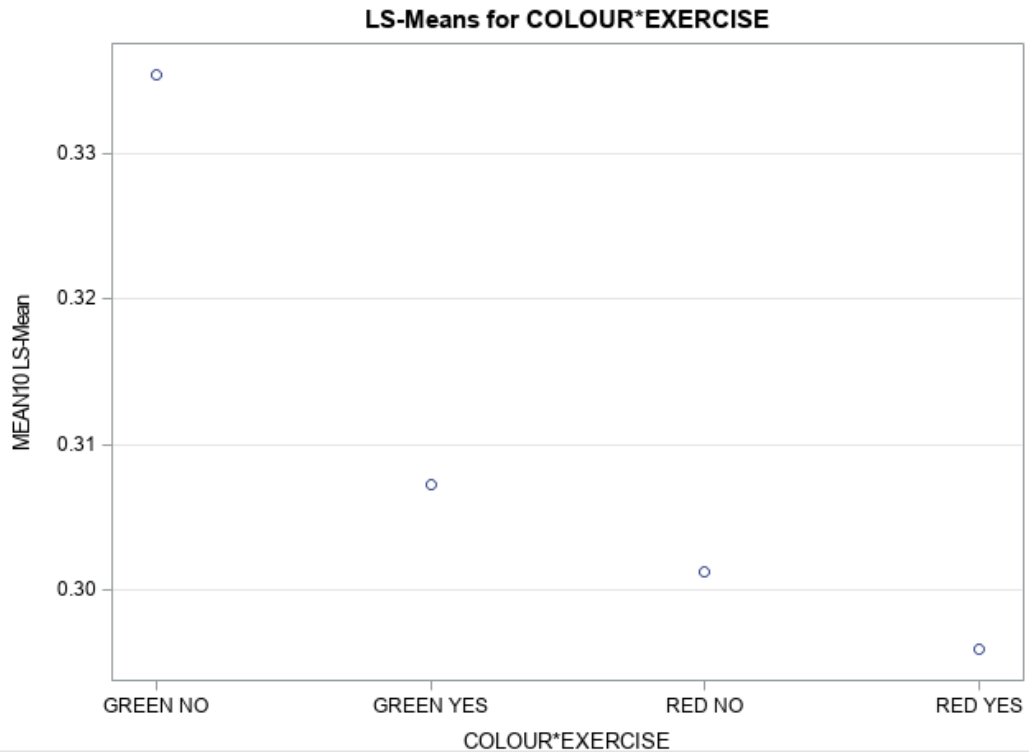
COLOUR	EXERCISE	MEAN10 LSMEAN	LSMEAN Number
GREEN	NO	0.33545250	1
GREEN	YES	0.30726750	2
RED	NO	0.30120042	3
RED	YES	0.29589083	4

Least Squares Means for Effect COLOUR*EXERCISE
t for H0: LSMean(i)=LSMean(j) / Pr > |t|
Dependent Variable: MEAN10

i/j	1	2	3	4
1		1.568359 0.1202	1.905963 0.0598	2.201416 0.0302
2	-1.56836 0.1202		0.337604 0.7364	0.633057 0.5283
3	-1.90596 0.0598	-0.3376 0.7364		0.295453 0.7683
4	-2.20142 0.0302	-0.63306 0.5283	-0.29545 0.7683	

Least Squares Means for Effect COLOUR*EXERCISE

i	j	Difference Between Means	95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.028185	-0.007507	0.063877
1	3	0.034252	-0.001440	0.069944
1	4	0.039562	0.003870	0.075254
2	3	0.006067	-0.029625	0.041759
2	4	0.011377	-0.024315	0.047069
3	4	0.005310	-0.030382	0.041002



SUBJECTS ALLOCATED USING A RANDOMIZED BLOCK DESIGN AND A **ONE WAY LAYOUT** OF TREATMENTS

```
PROC GLM DATA=REACTION  ;
CLASS GROUP ID ;
MODEL MEAN10 = GROUP ID / SS3 ;
LSMEANS GROUP/ADJUST=T      TDIFF PDIFF CL;
LSMEANS GROUP/ADJUST=TUKEY TDIFF PDIFF CL;
RUN ;
```

SUBJECTS ALLOCATED USING A RANDOMIZED BLOCK DESIGN AND A **ONE WAY LAYOUT** OF TREATMENTS

The GLM Procedure

Dependent Variable: MEAN10

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	26	0.32253265	0.01240510	15.18	<.0001
Error	69	0.05637493	0.00081703		
Corrected Total	95	0.37890758			

R-Square	Coeff Var	Root MSE	MEAN10 Mean
0.851217	9.221953	0.028584	0.309953

Source	DF	Type III SS	Mean Square	F Value	Pr > F
GROUP	3	0.02236293	0.00745431	9.12	<.0001
ID	23	0.30016972	0.01305086	15.97	<.0001

SUBJECTS ALLOCATED USING A RANDOMIZED BLOCK DESIGN AND A **ONE WAY LAYOUT** OF TREATMENTS

The GLM Procedure
Least Squares Means

GROUP	MEAN10 LSMEAN	LSMEAN Number
1	0.30726750	1
2	0.29589083	2
3	0.33545250	3
4	0.30120042	4

Least Squares Means for Effect GROUP
t for H0: LSMean(i)=LSMean(j) / Pr > |t|
Dependent Variable: MEAN10

i/j	1	2	3	4
1		1.378755 0.1724	-3.41578 0.0011	0.735279 0.4647
2	-1.37876 0.1724		-4.79454 <.0001	-0.64348 0.5220
3	3.415782 0.0011	4.794538 <.0001		4.151061 <.0001
4	-0.73528 0.4647	0.643476 0.5220	-4.15106 <.0001	

Least Squares Means for Effect GROUP

i	j	Difference Between Means	95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.011377	-0.005084	0.027838
1	3	-0.028185	-0.044646	-0.011724
1	4	0.006067	-0.010394	0.022528
2	3	-0.039562	-0.056023	-0.023101
2	4	-0.005310	-0.021771	0.011152
3	4	0.034252	0.017791	0.050713

P-value
0.1724
0.0011
0.4647
<.0001
0.5220
<.0001

SUBJECTS ALLOCATED USING A RANDOMIZED BLOCK DESIGN AND A **ONE WAY LAYOUT** OF TREATMENTS

The GLM Procedure
Least Squares Means
Adjustment for Multiple Comparisons: Tukey

GROUP	MEAN10 LSMEAN	LSMEAN Number
1	0.30726750	1
2	0.29589083	2
3	0.33545250	3
4	0.30120042	4

Least Squares Means for Effect GROUP
t for H0: LSMean(i)=LSMean(j) / Pr > |t|
Dependent Variable: MEAN10

i/j	1	2	3	4
1		1.378755 0.5168	-3.41578 0.0058	0.735279 0.8826
2	-1.37876 0.5168		-4.79454 <.0001	-0.64348 0.9175
3	3.415782 0.0058	4.794538 <.0001		4.151061 0.0005
4	-0.73528 0.8826	0.643476 0.9175	-4.15106 0.0005	

With Tukey adjustment p-values increase in order to allow for multiple comparisons

Least Squares Means for Effect GROUP

i	j	Difference Between Means	Simultaneous 95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.011377	-0.010347	0.033101
1	3	-0.028185	-0.049909	-0.006461
1	4	0.006067	-0.015657	0.027791
2	3	-0.039562	-0.061286	-0.017838
2	4	-0.005310	-0.027034	0.016414
3	4	0.034252	0.012528	0.055976

P-value
0.5168
0.0058
0.8826
<.0001
0.9175
0.0005

SUBJECTS ALLOCATED WITH A RANDOMIZED BLOCK DESIGN AND A 2 BY 2 FACTORIAL LAYOUT OF TREATMENTS

```
PROC GLM DATA=REACTION  ;
CLASS COLOUR EXERCISE ID ;
MODEL MEAN10 = COLOUR EXERCISE COLOUR*EXERCISE ID /SS3;
LSMEANS COLOUR          /ADJUST=T TDIFF PDIFF CL;
LSMEANS EXERCISE        /ADJUST=T TDIFF PDIFF CL;
LSMEANS COLOUR*EXERCISE/ADJUST=T TDIFF PDIFF CL;
RUN ;
```

AT LAST THIS IS WHAT HAPPENED !!

SUBJECTS ALLOCATED WITH A RANDOMIZED BLOCK DESIGN AND A 2 BY 2 FACTORIAL LAYOUT OF TREATMENTS

The SAS System

The GLM Procedure

Dependent Variable: MEAN10

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	26	0.32253265	0.01240510	15.18	<.0001
Error	69	0.05637493	0.00081703		
Corrected Total	95	0.37890758			

R-Square	Coeff Var	Root MSE	MEAN10 Mean
0.851217	9.221953	0.028584	0.309953

Source	DF	Type III SS	Mean Square	F Value	Pr > F
COLOUR	1	0.01249190	0.01249190	15.29	0.0002
EXERCISE	1	0.00673132	0.00673132	8.24	0.0054
COLOUR*EXERCISE	1	0.00313971	0.00313971	3.84	0.0540
ID	23	0.30016972	0.01305086	15.97	<.0001

SUBJECTS ALLOCATED WITH A RANDOMIZED BLOCK DESIGN AND A 2 BY 2 FACTORIAL LAYOUT OF TREATMENTS

The GLM Procedure
Least Squares Means

COLOUR	MEAN10 LSMEAN	H0:LSMean1=LSMean2	
		t Value	Pr > |t|
GREEN	0.32136000	3.91	0.0002
RED	0.29854563		

COLOUR	MEAN10 LSMEAN	95% Confidence Limits	
GREEN	0.321360	0.313129	0.329591
RED	0.298546	0.290315	0.306776

Least Squares Means for Effect COLOUR

i	j	Difference Between Means	95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.022814	0.011175	0.034454

The GLM Procedure
Least Squares Means

EXERCISE	MEAN10 LSMEAN	H0:LSMean1=LSMean2	
		t Value	Pr > |t|
NO	0.31832646	2.87	0.0054
YES	0.30157917		

EXERCISE	MEAN10 LSMEAN	95% Confidence Limits	
NO	0.318326	0.310096	0.326557
YES	0.301579	0.293349	0.309810

Least Squares Means for Effect EXERCISE

i	j	Difference Between Means	95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.016747	0.005108	0.028387

SUBJECTS ALLOCATED WITH A RANDOMIZED BLOCK DESIGN AND A 2 BY 2 FACTORIAL LAYOUT OF TREATMENTS

The GLM Procedure
Least Squares Means

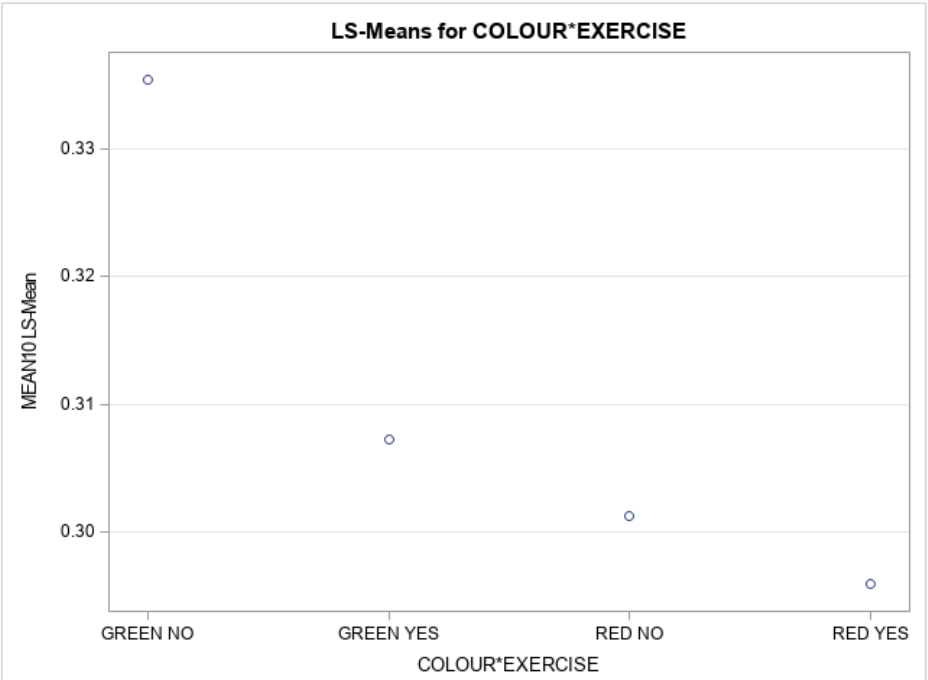
COLOUR	EXERCISE	MEAN10 LSMEAN	LSMEAN Number
GREEN	NO	0.33545250	1
GREEN	YES	0.30726750	2
RED	NO	0.30120042	3
RED	YES	0.29589083	4

Least Squares Means for Effect COLOUR*EXERCISE
t for H0: LSMean(i)=LSMean(j) / Pr > |t|
Dependent Variable: MEAN10

i/j	1	2	3	4
1		3.415782 0.0011	4.151061 <.0001	4.794538 <.0001
2	-3.41578 0.0011		0.735279 0.4647	1.378755 0.1724
3	-4.15106 <.0001	-0.73528 0.4647		0.643476 0.5220
4	-4.79454 <.0001	-1.37876 0.1724	-0.64348 0.5220	

Least Squares Means for Effect COLOUR*EXERCISE

i	j	Difference Between Means	95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.028185	0.011724	0.044646
1	3	0.034252	0.017791	0.050713
1	4	0.039562	0.023101	0.056023
2	3	0.006067	-0.010394	0.022528
2	4	0.011377	-0.005084	0.027838
3	4	0.005310	-0.011152	0.021771



*Tukey adjusted p = 0.0005

Suppose in a study that compared two drugs A and B, that drug A had better results.

BUT
1. A greater ***proportion*** of males than drug B
2. A younger mean age than drug B.
3. Smaller mean weight than drug B.

So, who cares? You should care if one or more of these variables are predictive of the outcome. A variable that is a predictor of the outcome and unevenly represented in the two groups is called a CONFOUNDER and if not included in the statistical analysis will lead to biased results.

ADVANTAGE OF THE GLM PROCEDURE OVER THE TTEST PROCEDURE

```
PROC GLM  DATA = DRUGS ;
CLASS DRUG SEX ;
MODEL  FVC  =  DRUG SEX AGE HEIGHT WEIGHT ;
LSMEANS DRUG ;
LSMEANS SEX ;
RUN ;
```

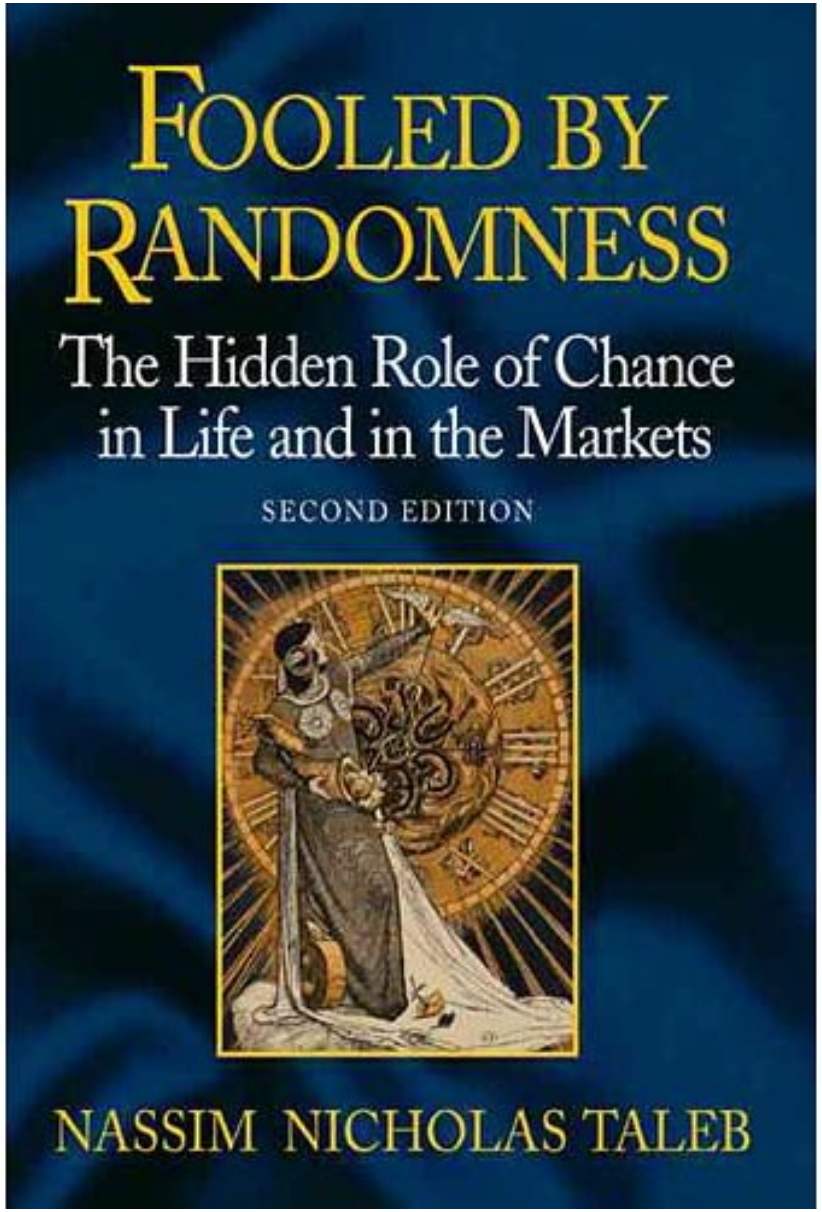
Researchers can include variables such as sex, age, height, and weight in the analysis

Suppose the p value associated with comparing the two means was 0.001. The critics ask " Were the groups comparable? "

What do they mean when they ask this question? I compared them didn't I? Isn't the p Value less than 0.05? Yes but with that observed difference I can rule out chance as the explanation for the difference.

I might be wrong but the smaller the p-value the stronger I feel about my conclusion. Even if there was a balance of these other predictors they would be included in the analysis because they would explain away some of the residual variation and make the p value associated with the drug effect smaller.

EVEN THEN I MAY HAVE BEEN FOOLED BY RANDOMNESS .


FOOLED BY RANDOMNESS
The Hidden Role of Chance in Life and in the Markets
SECOND EDITION
NASSIM NICHOLAS TALEB

STEP 1: Determine the p value for exposure variable DRUG.

STEP 2: Determine whether variables such as age and height are **predictors** of the outcome variable FVC. If so then including them in the data analysis will reduce the sampling variation and lower the p-value.

STEP 3: If in addition such predictor variables are unevenly represented in the two drug groups they are called **confounders** and the drug effect may be biased and correctly including them in the analysis may increase or decrease the estimated drug effect.

End of Lecture 2

Next up in Part 3 Lecture 1: Confounding